Notice of Allowability	Application No.	Applicant(s)	
	10/006,881	REITER ET AL.	
	Examiner	Art Unit	
	Stacy B Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *December 6, 2004*.

2. ☒ The allowed claim(s) is/are *1-9, 11-19 and 39-45*.

3. ☐ The drawings filed on _____ are accepted by the Examiner.

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

EXAMINER'S AMENDMENT

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 6, 2004 has been entered. *The quality of the amendment that was faxed/received on December 6, 2004 is poor and portions of all the claims are illegible. The examiner requested an electronic version of the claims in order to enter all of the claims in this examiner's amendment. Therefore, all pending claims in this application are listed below in the examiner's amendment.*

2. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Applicant's representative, Brigitte Hajos on February 11, 2005.

The application has been amended as follows:

IN THE CLAIMS:

Amend claim 1 to the following:

Claim 1 (currently amended): A method for production of virus comprising viral antigen, comprising the steps of (a) providing a culture of adherent cells bound to a microcarrier; (b) growing the cell culture to confluence; (c) infecting the cells with a virus; (d) incubating said culture of cells infected with said virus to propagate said virus, wherein the cell density of the biomass of the cell culture grown to confluence is increased by reduction of working volume (i)

prior to step (c) or (ii) after step (c) while the cells are bound to said microcarrier, and wherein the cell density is maintained at the increased cell density during step (d) as compared to the biomass grown to confluence during step (b); and (e) harvesting the virus produced.

Claim 2 (previously presented): The method according to claim 1, wherein the density of the cell culture grown to confluence is increased at least about 1.3 fold.

Claim 3 (previously presented): The method according to claim 1, wherein the cell density of the cell culture grown to confluence is between about 0.6×10^6 and about 7.0×10^6 cells/ml.

Claim 4 (previously presented): The method according to claim 1, wherein the microcarrier is selected from the group consisting of microcarriers made of dextran, collagen, polystyrene, polyacrylamide, gelatine, glass, cellulose, polyethylene and plastic.

Claim 5 (previously presented): The method according to claim 1, wherein the microcarrier concentration in the culture of cells of step (a) is between about 0.5 g/l and about 14 g/l.

Claim 6 (previously presented): The method according to claim 1, wherein said cells are selected from the group consisting of adherent cells of VERO, BHK, CHO, RK, RK44, RK13, MRC-5, MDCK, CEF and diploid monolayer cells.

Claim 7 (previously presented): The method according to claim 1, wherein said cells bound to a microcarrier are grown in serum free medium.

Claim 8 (previously presented): The method according to claim 1, wherein said cells bound to a microcarrier are grown in serum and protein free medium.

Amend claim 9 to the following:

Claim 9 (currently amended): The method according to claim 1, wherein the virus is selected from the group consisting of Influenza virus, Ross River Virus, Hepatitis A Virus, Vaccinia

Virus and recombinant Vaccinia Virus, Herpes Simplex Virus, Japanese encephalitis Virus, West Nile Virus, Yellow Fever Virus and chimeras thereof, Rhinovirus and Reovirus.

Claim 11 (previously presented): A method for production of purified virus or virus antigen comprising the steps of:

(a) providing a culture of adherent cells bound to a microcarrier;

(b) growing the cell culture to confluence;

(c) infecting the culture of cells with a virus;

(d) incubating said culture of cells infected with said virus to propagate said virus;

(e) harvesting the virus produced; and

(f) purifying said virus harvested, wherein the cell density of the biomass of the cell culture grown to confluence is increased by reduction of working volume (i) prior to step (c) or (ii) after step (c) while the cells are bound to said microcarrier, and wherein the cell culture is maintained at the increased cell density during step (d) as compared to the biomass grown to confluence during step (b).

Claim 12 (previously presented): The method according to claim 11, wherein the virus produced is harvested from the cell culture supernatant.

Claim 13 (previously presented): The method according to claim 11, wherein the virus produced is harvested from the cell biomass.

Amend claim 14 as follows:

Claim 14 (currently amended): A method for production of Influenza virus comprising viral antigen, comprising the steps of:

(a) providing a culture of adherent cells bound to a microcarrier;

(b) growing the cell culture to confluence;

(c) infecting the cells with an Influenza virus;

(d) incubating said culture of cells infected with said Influenza virus to propagate said virus, wherein the cell density of the biomass of the cell culture grown to confluence is

increased by reduction of working volume (i) prior to step (c) or (ii) after step (c) while the cells are bound to said microcarrier, and wherein the cell culture is maintained at the increased cell density during step (d) as compared to the biomass grown to confluence during step (b); and

(e) harvesting said Influenza virus produced.

Claim 15 (previously presented): The method according to claim 14, wherein said cells are VERO cells.

Claim 16 (previously presented): The method according to claim 14, wherein said cells are MDCK cells.

Claim 17 (previously presented): The method according to claim 14, wherein said cells bound to a microcarrier are grown in serum free medium.

Claim 18 (previously presented): The method according to claim 14, wherein said cells bound to a microcarrier are grown in serum and protein free medium.

Amend claim 19 to the following:

Claim 19 (currently amended): The method according to claim 14, wherein the cell culture grown to confluence is increased at least about 1.3 fold.

Cancel claim 21.

Claim 39 (previously presented): The method according to claim 1, wherein the cell culture in step (d) is maintained for at least three days.

Claim 40 (previously presented): The method according to claim 9, wherein the virus is Influenza virus.

Claim 41 (previously presented): The method according to claim 9, wherein the virus is Ross River Virus.

Amend claim 42 as follows:
Claim 42 (currently amended): The method according to claim 9, wherein the virus is selected from the group consisting of Vaccinia Virus and recombinant Vaccinia Virus.

Amend claim 43 as follows:
Claim 43 (currently amended): The method according to claim 9, wherein the virus is Japanese encephalitis Virus, West Nile Virus, Yellow Fever Virus or chimeras thereof.

Add claim 44:
Claim 44 (new): The method of claim 1, further comprising the step of purifying the virus or viral antigen.

Add claim 45:
Claim 45 (new): The method of claim 14, further comprising the step of purifying the Influenza virus or viral antigen.

Examiner's comment

3. Claims 1 and 14 were amended to clarify the difference between the use of the terms "virus" and "viral antigen". Claims 9 and 42 were amended to clarify the recombinant viruses being referred to. Claim 19 was amended to correct a grammatical error. Claim 21 was cancelled without prejudice. Claim 43 was amended to correct a grammatical error. Claims 44 and 45 were added in order to include the step of purifying virus or viral antigen. Support for amended claim 1 and new claim 44 is found on page 7, paragraph [029], lines 2 and 7 and page

8, paragraph [031], line 6. Support for amended claim 14 and new claim 45 is found on page 9, paragraph [033], lines 9-10. Support for amended claims 9 and 42 is found on page 6, paragraph [026], line 3.

Conclusion

4. Claims 1-9, 11-19 and 39-45 as amended are allowable.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30 EST). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James C. Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

James C. Housel 2/18/05

JAMES HOUSEL
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Stacy B. Chen
February 11, 2005

Complete Listing of Claims:

Claim 1 (currently amended): A method for production of virus comprising viral antigen, comprising the steps of (a) providing a culture of adherent cells bound to a microcarrier; (b) growing the cell culture to confluence; (c) infecting the cells with a virus; (d) incubating said culture of cells infected with said virus to propagate said virus, wherein the cell density of the biomass of the cell culture grown to confluence is increased by reduction of working volume (i) prior to step (c) or (ii) after step (c) while the cells are bound to said microcarrier, and wherein the cell density is maintained at the increased cell density during step (d) as compared to the biomass grown to confluence during step (b); and (e) harvesting the virus produced.

Claim 2 (previously presented): The method according to claim 1, wherein the density of the cell culture grown to confluence is increased at least about 1.3 fold.

Claim 3 (previously presented): The method according to claim 1, wherein the cell density of the cell culture grown to confluence is between about 0.6×10^6 and about 7.0×10^6 cells/ml.

Claim 4 (previously presented): The method according to claim 1, wherein the microcarrier is selected from the group consisting of microcarriers made of dextran, collagen, polystyrene, polyacrylamide, gelatine, glass, cellulose, polyethylene and plastic.

Claim 5 (previously presented): The method according to claim 1, wherein the microcarrier concentration in the culture of cells of step (a) is between about 0.5 g/l and about 14 g/l.

Claim 6 (previously presented): The method according to claim 1, wherein said cells are selected from the group consisting of adherent cells of VERO, BHK, CHO, RK, RK44, RK13, MRC-5, MDCK, CEF and diploid monolayer cells.

Claim 7 (previously presented): The method according to claim 1, wherein said cells bound to a microcarrier are grown in serum free medium.

Claim 8 (previously presented): The method according to claim 1, wherein said cells bound to a microcarrier are grown in serum and protein free medium.

Claim 9 (currently amended): The method according to claim 1, wherein the virus is selected from the group consisting of Influenza virus, Ross River Virus, Hepatitis A Virus, Vaccinia Virus and recombinant Vaccinia Virus, Herpes Simplex Virus, Japanese encephalitis Virus, West Nile Virus, Yellow Fever Virus and chimeras thereof, Rhinovirus and Reovirus.

Claim 10 (cancelled).

Claim 11 (previously presented): A method for production of purified virus or virus antigen comprising the steps of:

(a) providing a culture of adherent cells bound to a microcarrier;

(b) growing the cell culture to confluence;

(c) infecting the culture of cells with a virus;

(d) incubating said culture of cells infected with said virus to propagate said virus;

(e) harvesting the virus produced; and

(f) purifying said virus harvested, wherein the cell density of the biomass of the cell culture grown to confluence is increased by reduction of working volume (i) prior to step (c) or (ii) after step (c) while the cells are bound to said microcarrier, and wherein the cell culture is maintained at the increased cell density during step (d) as compared to the biomass grown to confluence during step (b).

Claim 12 (previously presented): The method according to claim 11, wherein the virus produced is harvested from the cell culture supernatant.

Claim 13 (previously presented): The method according to claim 11, wherein the virus produced is harvested from the cell biomass.

Claim 14 (currently amended): A method for production of Influenza virus comprising viral antigen, comprising the steps of:

(a) providing a culture of adherent cells bound to a microcarrier;

(b) growing the cell culture to confluence;

(c) infecting the cells with an Influenza virus;

(d) incubating said culture of cells infected with said Influenza virus to propagate said virus, wherein the cell density of the biomass of the cell culture grown to confluence is increased by reduction of working volume (i) prior to step (c) or (ii) after step (c) while the cells are bound to said microcarrier, and wherein the cell culture is maintained at the increased cell density during step (d) as compared to the biomass grown to confluence during step (b); and

(e) harvesting said Influenza virus produced.

Claim 15 (previously presented): The method according to claim 14, wherein said cells are VERO cells.

Claim 16 (previously presented): The method according to claim 14, wherein said cells are MDCK cells.

Claim 17 (previously presented): The method according to claim 14, wherein said cells bound to a microcarrier are grown in serum free medium.

Claim 18 (previously presented): The method according to claim 14, wherein said cells bound to a microcarrier are grown in serum and protein free medium.

Claim 19 (currently amended): The method according to claim 14, wherein the cell culture grown to confluence is increased at least about 1.3 fold.

Claims 20-38 (cancelled).

Claim 39 (previously presented): The method according to claim 1, wherein the cell culture in step (d) is maintained for at least three days.

Claim 40 (previously presented): The method according to claim 9, wherein the virus is Influenza virus.

Claim 41 (previously presented): The method according to claim 9, wherein the virus is Ross River Virus.

Claim 42 (currently amended): The method according to claim 9, wherein the virus is selected from the group consisting of Vaccinia Virus and recombinant Vaccinia Virus.

Claim 43 (currently amended): The method according to claim 9, wherein the virus is Japanese encephalitis Virus, West Nile Virus, Yellow Fever Virus or chimeras thereof.

Claim 44 (new): The method of claim 1, further comprising the step of purifying the virus or viral antigen.

Claim 45 (new): The method of claim 14, further comprising the step of purifying the Influenza virus or viral antigen.